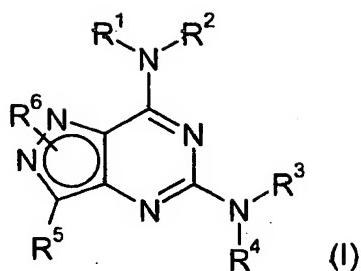


Claims

1. A compound of formula (I)



wherein

R¹ is a cyclic group selected from R^A, R^B, R^C and R^D, each of which is optionally substituted with one or more R⁷ groups;

R² is hydrogen or C₁-C₂ alkyl;

R³ and R⁴ are each independently C₁-C₆ alkyl, C₂-C₆ alkenyl, C₂-C₆ alkynyl or C₃-C₁₀ cycloalkyl, each of which is optionally substituted with one or more R^B groups, or R^E, which is optionally substituted with one or more R⁹ groups, or hydrogen;

or -NR³R⁴ forms R^F, which is optionally substituted with one or more R¹⁰ groups;

R⁵ is -Y-CONR¹⁵R¹⁶;

R⁶, which may be attached at N¹ or N², is C₁-C₆ alkyl, C₁-C₆ haloalkyl, C₂-C₆ alkenyl or C₂-C₆ alkynyl, each of which is optionally substituted by C₁-C₆ alkoxy, C₁-C₆ haloalkoxy or a cyclic group selected from R^J, R^K, R^L and R^M, or R⁶ is R^N, C₃-C₇ cycloalkyl or C₃-C₇ halocycloalkyl, each of which is optionally substituted by C₁-C₆ alkoxy or C₁-C₆ haloalkoxy, or R⁶ is hydrogen;

R⁷ is halo, C₁-C₆ alkyl, C₁-C₆ haloalkyl, C₂-C₆ alkenyl, C₂-C₆ alkynyl, C₃-C₁₀ cycloalkyl, C₃-C₁₀ halocycloalkyl, phenyl, OR¹², OC(O)R¹², NO₂, NR¹²R¹³, NR¹²C(O)R¹³, NR¹²CO₂R¹⁴, C(O)R¹², CO₂R¹², CONR¹²R¹³ or CN;

R⁸ is halo, phenyl, C₁-C₆ alkoxyphenyl, OR¹², OC(O)R¹², NO₂, NR¹²R¹³, NR¹²C(O)R¹³, NR¹²CO₂R¹⁴, C(O)R¹², CO₂R¹², CONR¹²R¹³, CN, R^G or R^H, the last two of which are optionally substituted with one or more R⁹ groups;

R⁹ is C₁-C₆ alkyl, C₁-C₆ haloalkyl or CO₂R¹²;

R¹⁰ is halo, C₃-C₁₀ cycloalkyl, C₃-C₁₀ halocycloalkyl, phenyl, OR¹², OC(O)R¹², NO₂, NR¹²R¹³, NR¹²C(O)R¹³, NR¹²CO₂R¹⁴, C(O)R¹², CO₂R¹³, CONR¹²R¹³, CN, oxo, C₁-C₆ alkyl or C₁-C₆ haloalkyl, the last two of which are optionally substituted by R¹¹;

R¹¹ is phenyl, NR¹²R¹³ or NR¹²CO₂R¹⁴;

R¹² and R¹³ are each independently hydrogen, C₁-C₆ alkyl or C₁-C₆ haloalkyl;

R¹⁴ is C₁-C₆ alkyl or C₁-C₆ haloalkyl;

R¹⁵ and R¹⁶ are each independently selected from

hydrogen,

C₁-C₆ haloalkyl,

C₁-C₆ alkyl optionally substituted with

R¹⁷,

-NR¹⁸R¹⁹,

-CO₂R²⁰,

-CONR²¹R²²,

R²³ or

phenyl optionally substituted by

halo,

C₁-C₆ alkyl or

R¹⁷,

C₃-C₇ cycloalkyl optionally substituted with

C₁-C₆ alkyl,

R¹⁷ or

-NR¹⁸R¹⁹, and

R²³;

or NR¹⁵R¹⁶ constitutes a 3- to 8-membered ring which may optionally include one or more further heteroatoms selected from nitrogen, oxygen and sulphur, and which may optionally be further substituted with R¹⁷, C₁-C₆ haloalkyl, -CO₂R²⁰, -CONR²¹R²², oxo or C₁-C₆ alkyl optionally substituted by R¹⁷;

R¹⁷ is hydroxy, C₁-C₆ alkoxy, C₁-C₆ (haloalkyl)oxy or C₃-C₇ cycloalkyloxy;

R¹⁸ and R¹⁹ are each independently selected from hydrogen and C₁-C₆ alkyl;

or -NR¹⁸R¹⁹ constitutes an azetidine, pyrrolidine, piperidine or morpholine ring;

R²⁰ is hydrogen or C₁-C₆ alkyl;

R²¹ and R²² are each independently selected from hydrogen, C₁-C₆ alkyl, C₁-C₆ haloalkyl and C₃-C₇ cycloalkyl;

or -NR²¹R²² constitutes a 3- to 8-membered ring which may optionally include one or more further heteroatoms selected from nitrogen, oxygen and sulphur;

R²³ is a saturated 3- to 8-membered ring which includes at least one heteroatom selected from nitrogen, oxygen and sulphur, which ring may optionally be substituted by one or more C₁-C₆ alkyl groups, provided that the group R²³ is joined to the parent molecule by a covalent bond to a carbon atom of said ring;

R^A and R^J are each independently a C₃-C₁₀ cycloalkyl or C₃-C₁₀-cycloalkenyl group, each of which may be either monocyclic or, when there are an appropriate number of ring atoms, polycyclic and which may be fused to either

(a) a monocyclic aromatic ring selected from a benzene ring and a 5- or 6-membered heteroaromatic ring containing up to three heteroatoms selected from nitrogen, oxygen and sulphur, or

(b) a 5-, 6- or 7-membered heteroalicyclic ring containing up to three heteroatoms selected from nitrogen, oxygen and sulphur;

R^B and R^K are each independently a phenyl or naphthyl group, each of which may be fused to

- (a) a C_5 - C_7 cycloalkyl or C_5 - C_7 cycloalkenyl ring,
- (b) a 5-, 6- or 7-membered heteroalicyclic ring containing up to three heteroatoms selected from nitrogen, oxygen and sulphur, or
- (c) a 5- or 6-membered heteroaromatic ring containing up to three heteroatoms selected from nitrogen, oxygen and sulphur;

R^C , R^L and R^N are each independently a monocyclic or, when there are an appropriate number of ring atoms, polycyclic saturated or partly unsaturated ring system containing between 3 and 10 ring atoms, of which at least one is a heteroatom selected from nitrogen, oxygen and sulphur, which ring may be fused to a C_5 - C_7 cycloalkyl or C_5 - C_7 cycloalkenyl group or a monocyclic aromatic ring selected from a benzene ring and a 5- or 6-membered heteroaromatic ring containing up to three heteroatoms selected from nitrogen, oxygen and sulphur;

R^D and R^M are each independently a 5- or 6-membered heteroaromatic ring containing up to three heteroatoms independently selected from nitrogen, oxygen and sulphur, which ring may further be fused to

- (a) a second 5- or 6-membered heteroaromatic ring containing up to three heteroatoms selected from nitrogen, oxygen and sulphur;
- (b) C_5 - C_7 cycloalkyl or C_5 - C_7 cycloalkenyl ring;
- (c) a 5-, 6- or 7-membered heteroalicyclic ring containing up to three heteroatoms selected from nitrogen, oxygen and sulphur; or
- (d) a benzene ring;

R^E , R^F and R^G are each independently a monocyclic or, when there are an appropriate number of ring atoms, polycyclic saturated ring system containing between 3 and 10 ring atoms, of which at least one is a heteroatom selected from nitrogen, oxygen and sulphur;

R^H is a 5- or 6-membered heteroaromatic ring containing up to three heteroatoms independently selected from nitrogen, oxygen and sulphur; and

Y is a covalent bond, C_1 - C_6 alkylene or C_3 - C_7 cycloalkylene;

a tautomer thereof or a pharmaceutically acceptable salt, solvate or polymorph of said compound or tautomer.

2. A compound according to claim 1 wherein R^1 is R^A , which is optionally substituted with one or more R^7 groups; and

R^A is a C_3 - C_{10} cycloalkyl group, which may be either monocyclic or, when there are an appropriate number of ring atoms, polycyclic, which may be fused to either

- (a) a monocyclic aromatic ring selected from a benzene ring and a 5- or 6-membered heteroaromatic ring containing up to three heteroatoms selected from nitrogen, oxygen and sulphur, or
- (b) a 5-, 6- or 7-membered heterocyclic ring containing up to three heteroatoms selected from nitrogen, oxygen and sulphur.

3. A compound according to claim 1 wherein R^1 is R^B , R^C , or R^D each optionally substituted with one or more R^7 groups, wherein

R^B is phenyl,

R^C is a monocyclic saturated or partly unsaturated ring system containing between 5 and 7 ring atoms, of which at least one is a heteroatom selected from nitrogen, oxygen and sulphur,

R^D is furanyl, thiienyl, pyrrolyl, pyrazolyl, imidazolyl, isoxazolyl, oxazolyl, isothiazolyl, thiazolyl, oxadiazolyl, pyridyl, pyridazinyl, pyrimidyl or pyrazinyl, and

R^7 is fluoro, methyl, ethyl, hydroxy, methoxy, propoxy or CONHMe.

4. A compound according to any one of claims 1 to 3 wherein R^2 is hydrogen or methyl.

5. A compound according to any one of claims 1 to 4 wherein R^3 is hydrogen or C_1-C_4 alkyl, which is optionally substituted with one or more R^8 groups, or R^3 is azetidinyl, pyrrolidinyl or piperidinyl, each of which is optionally substituted with one or more R^9 groups, wherein

R^8 is hydroxy, methoxy, methoxyphenyl, NH_2 , NHMe, NMe₂, NHCO₂Bu, NMeCO₂Bu, CO₂H, CONHMe, pyrrolidinyl, piperidinyl, morpholinyl or pyrazolyl, the last four of which are optionally substituted with one or more R^8 groups, and

R^9 is methyl or CO₂Bu.

6. A compound according to any one of claims 1 to 5 wherein R^4 is hydrogen, methyl or ethyl.

7. A compound according to any one of claims 1 to 6 wherein $-NR^3R^4$ forms R^F , which is optionally substituted with one or more R^{10} groups, wherein

R^F is selected from azetidinyl, pyrrolidinyl, piperidinyl, piperazinyl, morpholinyl, 3-azabicyclo[3.1.0]hex-3-yl, homopiperazinyl, 2,5-diazabicyclo[4.3.0]non-2-yl, 3,8-diazabicyclo[3.2.1]oct-3-yl, 3,8-diazabicyclo[3.2.1]oct-8-yl, 1,4-diazabicyclo[4.3.0]non-4-yl and 1,4-diazabicyclo[3.2.2]non-4-yl, and

R^{10} is halo, methyl, ethyl, isopropyl, hydroxy, methoxy, NH_2 , NHMe, NMe₂, NHCO₂Bu, CO₂H, CO₂Bu, oxo, benzyl, -CH₂NH₂, -CH₂NHMe, CH₂NMe₂ or -CH₂NMeCO₂Bu.

8. A compound according to any one of claims 1 to 7 wherein

R¹⁵ and R¹⁶ are each independently selected from hydrogen, C₁-C₆ alkyl optionally substituted with R¹⁷, -NR¹⁸R¹⁹, -CO₂R²⁰, -CONR²¹R²², R²³ or phenyl optionally substituted by halo, C₁-C₆ alkyl or R¹⁷, C₃-C₇ cycloalkyl and R²³, or NR¹⁵R¹⁶ constitutes a 5- to 7-membered ring which may optionally include one or more further heteroatoms selected from nitrogen and oxygen, and which may optionally be further substituted with R¹⁷, -CO₂R²⁰, -CONR²¹R²² or C₁-C₆ alkyl optionally substituted by R¹⁷;

R¹⁷ is hydroxy, C₁-C₆ alkoxy or C₃-C₇ cycloalkyloxy;

R²¹ and R²² are each independently selected from hydrogen, C₁-C₆ alkyl, and C₃-C₇ cycloalkyl, or -NR²¹R²² constitutes a 5- to 8-membered ring which may optionally include one or more further heteroatoms selected from nitrogen and oxygen; and

R²³ is a saturated 5- to 7-membered ring which includes at least one heteroatom selected from nitrogen and oxygen, which ring may optionally be substituted by one or more C₁-C₆ alkyl groups.

9. A compound according to any one of claims 1 to 8 wherein R⁶ is positioned on N¹.

10. A compound according to claim 9 wherein R⁶ is hydrogen, methyl, ethyl, isopropyl, isobutyl, methoxyethyl, methoxypropyl, ethoxyethyl, ethoxypropyl, propoxyethyl, 2,2,2-trifluoroethyl, tetrahydrofurylmethyl, tetrahydropyranyl methyl, tetrahydropyranyl or pyridinylmethyl.

11. A compound according to claim 1 wherein

R¹ is a cyclic group selected from R^A, R^B, R^C and R^D, each of which is optionally substituted with one or more R⁷ groups;

R⁷ is halo, C₁-C₆ alkyl, C₁-C₆ haloalkyl, OR¹² or CONR¹²R¹³;

R^B is halo, phenyl, C₁-C₆ alkoxyphenyl, OR¹², NR¹²R¹³, NR¹²CO₂R¹⁴, CO₂R¹², CONR¹²R¹³, R^G or R^H, the last two of which are optionally substituted with one or more R⁹ groups;

R^A is a monocyclic C₅-C₇ cycloalkyl group;

R^B is phenyl;

R^C is a monocyclic saturated ring system containing between 5 and 7 ring atoms, of which at least one is a heteroatom selected from nitrogen, oxygen and sulphur;

R^D is a 5-membered heteroaromatic ring containing a heteroatom selected from nitrogen, oxygen and sulphur and optionally up to two further nitrogen atoms in the ring, or a 6-membered heteroaromatic ring including 1, 2 or 3 nitrogen atoms;

R^E is a monocyclic saturated ring system containing between 3 and 7 ring atoms containing one nitrogen atom;

R^F is a monocyclic or, when there are an appropriate number of ring atoms, polycyclic saturated ring system containing between 3 and 10 ring atoms containing at least one nitrogen atom and optionally one other atom selected from oxygen and sulphur;

R^G is a monocyclic saturated ring system containing between 3 and 7 ring atoms, of which at least one is a heteroatom selected from nitrogen, oxygen and sulphur; and

R^H is a 5- or 6-membered heteroaromatic ring containing up to two nitrogen atoms.

R^3 is hydrogen, C_1 - C_4 alkyl, which is optionally substituted with one or more R^8 groups, or R^E , which is optionally substituted with one or more R^9 groups;

R^4 is hydrogen, C_1 - C_6 alkyl or C_1 - C_6 haloalkyl;

or $-NR^3R^4$ forms R^F , which is optionally substituted with one or more R^{10} groups;

R^6 is C_1 - C_4 alkyl or C_1 - C_4 haloalkyl, each of which is optionally substituted by C_1 - C_4 alkoxy, C_1 - C_4 haloalkoxy or a cyclic group selected from R^J , R^L and R^M , or R^6 is R^N or hydrogen;

R^J is cyclopropyl or cyclobutyl;

R^L and R^N are each independently a monocyclic saturated ring system containing either 5 or 6 ring atoms, of which at least one is a heteroatom selected from nitrogen, oxygen and sulphur;

R^M is a 5- or 6-membered heteroaromatic ring containing a heteroatom selected from nitrogen, oxygen and sulphur; and

Y is a covalent bond.

12. A compound according to claim 1 selected from:

1-(2-ethoxyethyl)-*N*-ethyl-5-(ethylamino)-7-(4-methylpyridin-2-ylamino)-1*H*-pyrazolo[4,3-*d*]pyrimidine-3-carboxamide,

5-(dimethylamino)-1-(2-ethoxyethyl)-*N*-methyl-7-(4-methylpyridin-2-ylamino)-1*H*-pyrazolo[4,3-*d*]pyrimidine-3-carboxamide,

5-(dimethylamino)-1-(2-ethoxyethyl)-*N*-(2-(methylamino)ethyl)-7-(4-methylpyridin-2-ylamino)-1*H*-pyrazolo[4,3-*d*]pyrimidine-3-carboxamide,

5-(dimethylamino)-*N*-(2-(dimethylamino)ethyl)-1-(2-ethoxyethyl)-7-(4-methylpyridin-2-ylamino)-1*H*-pyrazolo[4,3-*d*]pyrimidine-3-carboxamide,

5-(dimethylamino)-1-(2-ethoxyethyl)-7-(4-methylpyridin-2-ylamino)-*N*-(piperidin-4-yl)-1*H*-pyrazolo[4,3-*d*]pyrimidine-3-carboxamide,

5-(dimethylamino)-1-(2-ethoxyethyl)-*N*-(2-methoxyethyl)-7-(4-methylpyridin-2-ylamino)-1*H*-pyrazolo[4,3-*d*]pyrimidine-3-carboxamide,

(2*R*)-2-{{5-(dimethylamino)-1-(2-ethoxyethyl)-7-(4-methylpyridin-2-ylamino)-1*H*-pyrazolo[4,3-*d*]pyrimidine-3-carbonyl]amino}propionic acid,

3-{{5-(dimethylamino)-1-(2-ethoxyethyl)-7-(4-methylpyridin-2-ylamino)-1*H*-pyrazolo[4,3-*d*]pyrimidine-3-carbonyl]amino}propionic acid,

1-(2-ethoxyethyl)-*N*-methyl-7-(4-methylpyridin-2-ylamino)-5-(piperazin-1-yl)-1*H*-pyrazolo[4,3-*d*]pyrimidine-3-carboxamide,

1-(2-ethoxyethyl)-*N*-methyl-5-((3*R*)-3-methylpiperazin-1-yl)-7-(4-methylpyridin-2-ylamino)-1*H*-pyrazolo[4,3-*d*]pyrimidine-3-carboxamide,

1-(2-ethoxyethyl)-*N*-ethyl-5-((3*R*)-3-methylpiperazin-1-yl)-7-(4-methylpyridin-2-ylamino)-1*H*-pyrazolo[4,3-*d*]pyrimidine-3-carboxamide,

1-(2-ethoxyethyl)-5-(ethylamino)-N-methyl-7-(4-methylpyridin-2-ylamino)-1*H*-pyrazolo[4,3-*d*]pyrimidine-3-carboxamide,

1-(2-ethoxyethyl)-*N*-(2-methoxyethyl)-5-(methylamino)-7-(4-methylpyridin-2-ylamino)-1*H*-pyrazolo[4,3-*d*]pyrimidine-3-carboxamide,

5-(dimethylamino)-1-(2-ethoxyethyl)-*N*-(2-hydroxyethyl)-7-(4-methylpyridin-2-ylamino)-1*H*-pyrazolo[4,3-*d*]pyrimidine-3-carboxamide,

1-(2-ethoxyethyl)-5-(ethylamino)-*N*-(2-methoxyethyl)-7-(4-methylpyridin-2-ylamino)-1*H*-pyrazolo[4,3-*d*]pyrimidine-3-carboxamide,

1-(2-ethoxyethyl)-5-(*N*-(2-hydroxyethyl)-*N*-methylamino)-*N*-methyl-7-(4-methylpyridin-2-ylamino)-1*H*-pyrazolo[4,3-*d*]pyrimidine-3-carboxamide,

1-(2-ethoxyethyl)-5-((2-methoxyethyl)amino)-*N*-methyl-7-(4-methylpyridin-2-ylamino)-1*H*-pyrazolo[4,3-*d*]pyrimidine-3-carboxamide,

7-(cyclohexylamino)-1-(2-ethoxyethyl)-*N*-methyl-5-((3*R*)-3-methylpiperazin-1-yl)-1*H*-pyrazolo[4,3-*d*]pyrimidine-3-carboxamide, and

1-(2-ethoxyethyl)-*N*-methyl-5-[*N*-methyl-*N*-((3*S*)-1-methylpyrrolidin-3-yl)amino]-7-(4-methylpyridin-2-ylamino)-1*H*-pyrazolo[4,3-*d*]pyrimidine-3-carboxamide

and tautomers thereof and pharmaceutically acceptable salts, solvates and polymorphs of said compound or tautomer.

13. A pharmaceutical composition comprising a compound of formula (I) as claimed in any one of claims 1 to 12, or pharmaceutically acceptable salts, solvates or polymorphs thereof, and a pharmaceutically acceptable diluent or carrier.

14. A compound of formula (I) as claimed in any one of claims 1 to 12, or a pharmaceutically acceptable salt, solvate or polymorph thereof, for use as a medicament for the treatment of a disease or condition selected from hypertension (including essential hypertension, pulmonary hypertension, secondary hypertension, isolated systolic hypertension, hypertension associated with diabetes, hypertension associated with atherosclerosis, and renovascular hypertension), congestive heart failure, angina (including stable, unstable and variant (Prinzmetal) angina), stroke, coronary artery disease, congestive heart failure, conditions of reduced blood vessel patency (such as post-percutaneous coronary angioplasty), peripheral vascular disease, atherosclerosis, nitrate-induced tolerance, nitrate tolerance, diabetes, impaired glucose tolerance, metabolic syndrome, obesity, sexual dysfunction (including male erectile disorder, impotence, female sexual arousal disorder, clitoral dysfunction, female hypoactive sexual desire disorder, female sexual pain disorder, female sexual orgasmic dysfunction and sexual dysfunction due to spinal cord injury), premature labour, pre-eclampsia, dysmenorrhea, polycystic ovary syndrome, benign prostatic hyperplasia, bladder outlet obstruction, incontinence, chronic obstructive pulmonary disease, acute respiratory failure, bronchitis, chronic asthma, allergic asthma, allergic rhinitis, gut motility disorders (including irritable bowel syndrome), Kawasaki's syndrome, multiple sclerosis, Alzheimer's disease, psoriasis, skin necrosis, scarring, fibrosis, pain (particularly neuropathic pain), cancer, metastasis, baldness, nutcracker oesophagus, anal fissure and haemorrhoids.

15. Use according to claim 14 wherein the disease or condition is selected from essential hypertension, pulmonary hypertension, secondary hypertension, isolated systolic hypertension, hypertension associated with diabetes, hypertension associated with atherosclerosis, and renovascular hypertension.